IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:	Confirmation No.: 6701
Meng YANG et al.	Group Art Unit: 1633
Serial No.: 10/775,554	Examiner: Anne Marie Sabrina Wehbé, Ph.D.
Filing Date: February 9, 2004	
For: IMMUNOCOMPROMISED RODENTS AS DUAL COLOR TUMOR MODELS	

DECLARATION OF ROBERT M. HOFFMAN
UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, Robert M. Hoffman, declare as follows:

1. I am President of AntiCancer, Inc., the assignee of the herein application. I have worked closely with the model systems claimed in the present application and am aware of the properties of the rodents obtained in our laboratories by the present inventors.

2. It is understood in the art that in order to be used as a model system for foreign tumor growth, a laboratory animal must be immunocompromised. Immunocompromised rodents such as nu/nu mice are routinely used for this purpose.

3. The inventors in the present application, who work in the laboratories of AntiCancer, believed that it would be advantageous to visualize fluorescent tumors and their metastases in such model systems if the host system itself were ubiquitously fluorescent. Thus, greater contrast could be obtained between the tumor or the metastases and the background tissues of the host. Therefore, they considered using, for example, the fluorescent mouse of Okabe cited in the present prosecution as an appropriate starting point, provided that this mouse could be immunocompromised and also be receptive to foreign tumor tissue without deleterious effects.

4. In attempting to prepare such a model system, the Okabe mice were bred with immunocompromised nu/nu mice. In the second generation (*i.e.*, the first generation that would have members that were immunocompromised among the progeny) both homozygous and heterozygous offspring with respect to the fluorescence-creating gene were obtained. Surprisingly, it was observed that the homozygous offspring that were immunocompromised were unable to tolerate the implantation of foreign tumors. Therefore, the inventors concluded it would be necessary to crossbreed these offspring, some of which are homozygous for the fluorescence, with a immunocompromised parent that did not express the fluorescent protein. All of the offspring of this generation that exhibited fluorescence were heterozygous, and thus useful in studies as host tumor models.

5. Prior to this work, it was not understood that heterozygosity of the fluorescence gene ubiquitously expressed in all tissues was a requirement for use of this system as a tumor model.

I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further, that these statements are made with the knowledge that willful, false statements and the like so made are punishable by

fine or imprisonment or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Executed at San Diego, California on 22 (day) April 2011.

Robert M. Hoffman